

WHAT IS CLAIMED IS:

1. A stent having a coating comprising:
  - (a) a primer layer comprising a plurality of polymers comprising an anchoring polymer, and
  - (b) a drug reservoir layer comprising a polymeric matrix of a second composition of a plurality of polymers, comprising a drug stabilizing polymer and a toughening polymer, the first composition being distinct from the second composition, and one or more active agents integrated in the polymer matrix, the polymeric matrix protecting and stabilizing the one or more active agents during sterilization and storage,  
the coating having sufficient adhesion and flexibility to remain intact upon insertion and stent expansion in a subject and releasing efficacious amounts of the active agent at the site of stent expansion.
- 15 2. The stent of claim 1, further comprising an intermediate layer between the primer layer and the drug release layer, comprising a polymer composition distinct from the first and second compositions.
- 20 3. The medicated stent of claim 1, further comprising one or more image enhancing material(s) in one of the layers, or in a separate layer(s), that is capable of enhancing visibility in ultra sound, magnetic resonance imaging, or X ray imaging.
4. The stent of claim 1, wherein the primer layer and/or the drug reservoir layer is a single layer.
- 25 5. The stent of claim 1, wherein the anchoring polymers have functional groups, selected from amides, carboxyl, hydroxyl, amine, imine, amide, imide, sulfoxyl, sulfonyl, and combinations.
6. The stent of claim 1, wherein the primer layer further comprises one or more cross-linking and/or cross-linkable polymers selected from epoxy resins, melamine resins, phenolics, and isocyanate polymers.
- 30 7. The stent of claim 1, wherein the primer layer further comprises one or more of polyvinylpyrrolidone/vinyl acetate copolymer (PVP/VA), olefin acrylic acid copolymer, polyethylene glycol, polyethylene oxide, and polyvinylpyridine polymers and copolymers.
8. The stent of claim 1, wherein the stabilizing polymer is a cellulose ester, a

cellulose ether, an acrylic polymer and/or an acrylic copolymer.

9. The stent of claim 1 wherein the toughening polymer is a polyurethane.

10. The stent of claim 1 wherein the drug reservoir layer further includes a relatively hydrophilic polymer selected from the group consisting of hydroxyethyl 5 methacrylate, acrylic HEMA (polyhydroxyethyl methacrylate/methylmethacrylate) copolymers, polyvinyl pyrrolidone, polyvinylpyrrolidone/vinyl acetate copolymers (PVP/VA), polyethylene glycols, and polyethylene oxides.

11. The stent of claim 1 comprising more than one active agent.

12. The stent of claim 1 in which the primer layer comprises one or more 10 polymers selected from the group consisting of acrylate polymer/copolymer, acrylate carboxyl and/or hydroxyl copolymer, olefin acrylic acid copolymer, ethylene acrylic acid copolymer, polyamide polymers/copolymers polyimide polymers/copolymers, and/or polyether sulfones.

13. The stent of claim 1 in which the primer layer comprises one or more 15 polymers selected from the group consisting of ethylene vinylacetate copolymer, acrylate polymer/copolymer, acrylate carboxyl and/or hydroxyl copolymer, olefin acrylic acid copolymer, ethylene acrylic acid copolymer, polyamide polymers/copolymers polyimide polymers/copolymers, and/or polyether sulfones.

14. The stent of claim 2, wherein the intermediate layer comprises one or more 20 polymers selected from the group consisting of acrylate polymer/copolymer, acrylate carboxyl and/or hydroxyl, polyvinylpyrrolidone/vinyl acetate copolymer (PVP/VA), polyurethane, silicone urethane polymer, polycarbonate urethane polymer, polyvinylbutyral, and/or epoxy polymers.

15. The stent of claim 1, wherein the primer and/or drug reservoir layer 25 comprises one or more polymer selected from the group consisting of polyurethane, polycarbonate urethane polymer, and silicone urethane polymer.

16. The stent of claim 1 comprising one or more polymers having a flexural modulus greater than 1000 psi and elongation at break greater than 200%.

17. The stent of claim 1 having a drug reservoir layer comprising a polymer 30 selected from acrylate polymer/copolymer, acrylate hydroxyl and/or carboxyl copolymer, polyvinyl pyrrolidone (PVP), polyvinylpyrrolidone/vinyl acetate copolymer (PVP/VA), cellulose ester, polyurethane, polycarbonate-urethane polymer, silicone-urethane polymer, epoxy polymer, polyethylene glycol and/or polyethylene oxide.

18. The stent of claim 1 having a drug reservoir layer comprising one or more polyurethanes, and one or more cellulose ester polymers.

19. The stent of claim 1 having a drug reservoir layer comprising one or more polymers selected from acrylate polymer/copolymer, acrylate polymer/copolymer containing 5 carboxyl and/or hydroxyl groups, cellulose nitrate and/or other cellulose ester.

20. The stent of claim 1 wherein the active agent comprises an anti-restenotic agent effective at a stented site.

21. The stent of claim 1 having a total coating thickness between about 0.3 and about 30 microns.

10 22. The stent of claim 1 the primer layer having a thickness between about 0.01 and about 5 microns, and the drug reservoir layer having a thickness of between about 0.1 and about 10 microns.

23. The stent of claim 2 the intermediate layer having a thickness between about 0.1 and about 15 microns.

15 24. The stent of claim 1 wherein the active agent is selected from one or more of anti-thrombogenic agents, anti-inflammatory agents, antineoplastic agents, anti-proliferative agents, cytostatic agents, cytotoxic agents, antimicrobial agents, anti-restenotic agents, anti-platelet agents, and anti-coagulant agents.

20 25. The stent of claim 1 wherein the active agent is selected from one or more of anti-fibrin and fibrinolytic agents, anti-platelet agents, prostacyclins (and analogues), glycoprotein IIb/IIIa agents, thromboxane inhibitors, anti-thrombin and anti-coagulant agents, anti-mitotic, antiproliferative and cytostatic agents, antiangiogenic and angiostatic agents, ACE inhibitors, growth factor antagonists, antioxidants, vitamins, calcium channel blockers, fish oil (omega 3-fatty acid), phosphodiesterase inhibitors, nitric acid donor, 25 Somatostatin analogues, immunosuppressive agents, antiinflammatory agents, antimicrobials, radionuclides including alpha, beta and gamma emitting isotopes, COX-2 inhibitors, endothelial promoters, kinase inhibitors, epidermal growth factor kinase inhibitors, tyrosine kinase inhibitors, MAP kinase inhibitors, and protein transferase inhibitors.

30 26. The stent of claim 1 wherein the active agent is selected from one or more of plasmin, streptokinase, single chain urokinase, urokinase, t-PA (tissue type plasminogen activator), aminocaproic acid, aspirin, monoclonal antibodies, peptides, ReoPro, Cilastagel, eptifibatide, tirofiban, ticlopidine, Vapiprost, dipyridamole, forskolin, angiopeptin, argatroban, dextan, heparin, LMW heparin, heparin complexes, Enoxaparin, Dalteparin,

hirudin, recombinant hirudin, anti-thrombin, synthetic antithrombins, thrombin inhibitors, Warfarin, other coumarins, vincristine, vinblastine, paclitaxel and its analogues, methotrexate, cisplatin, fluorouracil, rapamycin, azathioprine, cyclophosphamide, mycophenolic acid, corticosteroids, colchicine, nitroprusside, paclitaxel, angiostatin and 5 endostatin; genetic materials, oligonucleotides, Cilazapril, Lisinopril, Captopril, VEGF, FGF, Probucol, Tocopherol, nifedipine, dipyridamole, Molsidomine, angiopeptin, prednisolone, glucocorticoid, dexamethasone, rifamycin, Re-188, Re-186, I-125, Y-90 celecoxib, Vioxx, dipyridamole, and theophylline.

27. The stent of claim 1 wherein the active agent is selected from one or more 10 of tacrolimus, everolimus, sirolimus, plasmin, streptokinase, single chain urokinase, urokinase, t-PA (tissue type plasminogen activator), aminocaproic acid, aspirin, monoclonal antibodies, peptides, ReoPro, Cilastagel, eptifibatide, tirofiban, ticlopidine, Vapiprost, dipyridamole, forskolin, angiopeptin, argatroban, dextan, heparin, LMW heparin, heparin complexes, Enoxaparin, Dalteparin, hirudin, recombinant hirudin, anti-thrombin, synthetic 15 antithrombins, thrombin inhibitors, Warfarin, other coumarins, vincristine, vinblastine, paclitaxel and its analogues, methotrexate, cisplatin, fluorouracil, rapamycin, azathioprine, cyclophosphamide, mycophenolic acid, corticosteroids, colchicine, nitroprusside, paclitaxel, angiostatin and endostatin; genetic materials, oligonucleotides, Cilazapril, Lisinopril, Captopril, VEGF, FGF, Probucol, Tocopherol, nifedipine, dipyridamole, Molsidomine, 20 angiopeptin, prednisolone, glucocorticoid, dexamethasone, rifamycin, Re-188, Re-186, I-125, Y-90 celecoxib, Vioxx, dipyridamole, and theophylline.

28. The stent of claim 1 wherein the primer layer comprises one or more of acrylate/carboxyl polymer, epoxy polymer, polyvinylpyrrolidone vinylacetate copolymer (PVP/VA).

25 29. The stent of claim 1 wherein the primer layer comprises one or more of ethylene acrylic acid copolymer (EAA), epoxy polymer, and polycarbonate urethane.

30. The stent of claim 2 wherein the intermediate layer comprises polycarbonate polyurethane.

31. The stent of claim 1 wherein the drug reservoir layer comprises one or more 30 of acrylate/carboxyl polymer, epoxy polymer, and polyvinylpyrrolidone vinylacetate copolymer (PVP/VA).

32. The stent of claim 1 wherein the drug release layer comprises nitrocellulose.

33. The stent of claim 1 wherein the drug release layer comprises nitrocellulose and one or more of polytetramethylene ether glycol urethane, polycarbonate-urethane, silicone-urethane polymer, polyethylene glycol, polymethylmethacrylate-2-hydroxyethylmethacrylate copolymer, polyethylmethacrylate-2-hydroxyethylmethacrylate 5 copolymer, polypropylmethacrylate-2-hydroxyethylmethacrylate copolymer, polybutylmethacrylate-2-hydroxyethylmethacrylate copolymer, Polymethylacrylate-2-hydroxyethylmethacrylate copolymer, polyethylacrylate-2-hydroxyethylmethacrylate copolymer, polypropylacrylate-2-hydroxymethacrylate copolymer, polybutylacrylate-2-hydroxyethylmethacrylate copolymer, copolymermethylvinylether maleicanhydride 10 copolymer, and poly (2-hydroxyethyl methacrylate).

34. The stent of claim 1, wherein the drug release layer comprises an ionic heparin complex, and at least one other bioactive agent that is not anti-thrombogenic.

35. The stent of claim 1, wherein one of the agents is an ionic complex of heparin, and at least one more agent is present that is selected from the group consisting of 15 an anti-angiogenic factor, an immunosuppressing agent, an antimicrobial agent, an anti-inflammatory agent, an anti-restenotic agent and combinations.

36. The stent of claim 1, wherein the active agent comprises heparin together with at least one of an anti-restenotic drug selected from the group consisting of paclitaxel, rapamycin, sirolimus, everolimus, tacrolimus, and combinations.

20 37. The stent of claim 1 wherein the active agent is selected from the group consisting of paclitaxel, heparin complexes, rifamycin, methotrexate, and combinations.

38. The stent of claim 1, wherein the active agents are benalkoniumheparinate and paclitaxel.

25 39. The stent of claim 1, wherein the primer layer comprises an ethylene acrylic acid copolymer and an epoxy polymer.

40. The stent of claim 39, wherein the ethylene acrylic acid copolymer is one or more of PRIMACOR.TM. 5989 and 5990.

41. The stent of claim 39, wherein the epoxy is one or more of EPOTUF.RTM. 38-505, EPOTUF.RTM. 37-618, and EPON 1001.

30 42. The stent of claim 1, wherein the drug reservoir layer comprises a polyurethane and a cellulose nitrate.

43. The stent of claim 42, wherein the polyurethane is polytetramethylene ether glycol urethane and/or polycarbonate urethane.

44. The stent of claim 42 wherein the polyurethane is selected from the group consisting of Chronoflex AR, Chronoflex AL, Chronoflex C and Bionate 80A.

45. The stent of claim 42 wherein the polyurethane is Chronoflex AR.

46. The stent of claim 1, wherein the primer layer comprises an ethylene acrylic acid copolymer and an epoxy polymer and the drug reservoir layer comprises a polyurethane and a cellulose ester.

47. A stent comprising:

a stent body,

a biologically active agent,

means for containing and controllably releasing the agent from the stent over an extended period, comprising a means for stabilizing the active agent and means for strengthening the containing means, and

means for anchoring the containing means to the stent body, comprising a second polymer,

the containing and anchoring means remaining intact upon stent expansion and during the extended period.

48. A method for making a stent having struts, comprising:

applying a primer polymer liquid comprising a first polymer in a first volatile medium,

removing the first volatile medium to form a primer layer without forming coating bridges between struts of the stent ,

applying a drug reservoir polymer liquid comprising at least two polymers in a second volatile medium and an active agent, the at least two drug reservoir polymers being different from the at least two primer layer polymers,

removing the second volatile medium to form a drug reservoir layer without forming coating bridges between struts of the stent, and

the layers remaining intact upon stent expansion, and releasing efficacious amounts of the active agent at the site of stent expansion.